

REMARKS

Applicant expresses appreciation to the Examiner for consideration of the subject patent application. This amendment and remarks are in response to the Office Action mailed January 21, 2011 in which each of pending claims 73-89 and 92-116 were rejected. For the Examiner's convenience and reference, Applicants' remarks are presented in the order in which the corresponding issues were raised in the Office Action.

In the office action of January 21, 2011, the following actions were taken:

- (1) Claims 73-89 and 92-116 were rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement;
- (2) Claim 116 was rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the enablement requirement;
- (3) Claims 73, 76-89, 92-99, and 107-115 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent Application No. 2003/0170307 (hereinafter "Royer"), WO 03/065996 (hereinafter "Wise"), and U.S. Patent. No. 6,479,418 (hereinafter "Li");
- (4) Claims 74-75 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Royer, Wise, and Li, and further in view of U.S. Patent No. 5,162,117 (hereinafter "Stupak"); and
- (5) Claims 100-106 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Royer, Wise, and Li, and further in view of U.S. Publication No. 2003/0158598 (hereinafter "Ashton").

Claim Amendments

By the present amendment, Claims 73, 75, and 116 have been amended to remove the terms "prophylactically," "derivative," and "analog" from the claims. Claim 73 has further been amended to include the limitations of previously presented claim 98, which has subsequently been canceled, to include a specific range for expandable agent as disclosed in the specification, page 11, line 2, and to be injectable as disclosed in the specification, page 4, lines 35-36. Applicants

submit that the present amendments are fully supported by the originally filed specification and that they do not introduce any new subject matter.

Claim Rejections - 35 U.S.C. § 112

Claims 73-89 and 92-116 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Specifically, the Examiner has asserted that the claims use overly broad terms including “derivative” and “analog.” Additionally, claim 116 was rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Specifically, the Examiner has asserted that the present specification does not provide enablement for “prophylactically active substances.”

Without conceding the correctness of the Examiner’s rejection, Applicants have amended the claims to remove all language regarding the prophylactic use of the claimed substances and the objected to terms “derivative” and “analog.” Accordingly, Applicants submit that the rejection is rendered moot and request its withdrawal.

Claim Rejections - 35 U.S.C. § 103

Claims 73, 76-89, 92-99, and 107-115 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Royer, Wise, and Li.

Before discussing the obviousness rejections herein, it is thought proper to briefly state what is required to sustain such a rejection. The issue under § 103 is whether the PTO has stated a case of *prima facie* obviousness. The Applicant does not deem it necessary to recite the entire case law standard required in order to establish a *prima facie* case of obviousness. However, the Applicant would like to briefly remind the Examiner that a *prima facie* case of obviousness generally includes establishing: 1) that the asserted references as modified or combined teach or suggest each and every element of the claimed invention, 2) that the asserted references as modified or combined provide a sufficient likelihood of successfully making the modification or combination, and 3) a reason for the modification or combination asserted.

Additionally, under *KSR*, and as outlined under the MPEP § 2143, additional rationales include (a) combining prior art elements according to known methods to yield predictable results; (b) simple substitution of one known element for another to obtain predictable results; (c) use of

known technique to improve similar devices (methods, or products) in the same way; (d) applying a known technique to a known device (method, or product) ready for improvement to yield predictable results; (e) "obvious to try" - choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success; (f) known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art; and (g) some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention. The Applicant respectfully asserts the Examiner has not satisfied the requirement for establishing a case of *prima facie* obviousness in any of the rejections.

First, Applicants note that claim 73 has been amended to include the limitations of previously presented claim 98 and a specific concentration of the expandable agent, namely about 0.1 % w/w to about 2.5% w/w. The Applicant note that these elements have been added in accordance with experimental results submitted in a declaration concurrently herewith.

The declaration submitted herewith provides experimental results of 3 pastes with differing amounts of sodium bicarbonate, an expandable agent, with water and calcium sulphate according to Table 1.

Table 1

| Components | Paste 1 | Paste 2 | Paste 3 |
|---|---------|---------|---------|
| Calcium Sulphate ($\text{CaSO}_4 \cdot 1/2\text{H}_2\text{O}$ from Riedel-deHaen) (wt%) | 59.41 | 54.55 | 46.15 |
| NaHCO_3 (wt%) | 0.59 | 5.45 | 13.85 |
| Water (deionized) (wt%) | 40 | 40 | 40 |
| Total (wt%) | 100 | 100 | 100 |

| | | | |
|-----------|-------------|--------|-------------------------|
| Cure Time | 3-5 minutes | 1 hour | Not cured after 3 hours |
|-----------|-------------|--------|-------------------------|

As shown in Table 1, the varying amounts of sodium bicarbonate greatly affected the cure times of the pastes, differing by at least an order of magnitude between Paste 1 and the other pastes. Applicants submit that the present results show that the present compositions having an expandable agent between about 0.1% w/w to about 2.5% w/w, a sorbed aqueous medium between about 30% w/w and about 60% w/w, with a biodegradable hydrating ceramic provide an unexpected cure time not predicted by the prior art.

To be clear, the Applicants note that the sodium bicarbonate cited in Royer is present in its composition in an amount from 5% to about 15% as disclosed in Example 15, paragraphs [0147] and [0150]. As such, Applicants note that Royer does not teach or disclose the presently recited amounts of an expandable agent. Perhaps more importantly, based on the above, the Applicants note that such amounts would not be expected to provide the presently claimed cure time of less than 20 minutes. To reiterate, Applicants have amended the present claims to reflect the unexpected results provided by the present formulations.

Further, Applicants note that the present experimental results show that the expandable agent is a result effective variable for the presently claimed cure times while the prior art provides no teaching that the expandable agent can be used to achieve or affect the cure times. With regards to optimization, the Applicants note that the Examiner has previously argued that optimization would be possible by one skilled in the art “absent evidence of criticality.” However, as discussed above, Applicants note that the present experimental results show that the amounts recited in the present claims are critical to achievement of the claimed curing time. As such, Applicants submit that one skilled in the art would not optimize the present compositions to the presently claimed amounts as the effects of such amounts were unknown to affect the curing time as discovered by the present inventors.

Further, Applicants maintain that Royer does not even use the term “expandable agent” or anything akin to such a term, but rather only coincidentally discloses in a single example with a single compound (i.e. sodium bicarbonate) that falls within the scope of expanding agents claimed in the present invention. In fact, Royer does not even discuss or disclose the functionality or

purpose of the sodium bicarbonate that is present in the example, let alone mention a specific reason for the amounts recited. In short, nothing in Royer supports the Examiner's allegation that the present ranges recited would be merely routine obvious optimization of the amounts of the compound. Applicants contend that optimization of the amount of expandable agent cannot be done when the role of the expandable agent is not even recognized. One of ordinary skill in the art cannot optimize a variable that they do not recognize as result effective. Ergo, one of ordinary skill in the art would not be able to optimize the amount of an expandable agent when there is no recognition of the role of the expandable agent, or that a stated substance acts as an expandable agent. The mere showing that a composition exists in the art that happens to disclose a compound that in hindsight can be used, in the correct amounts, as an expandable agent is insufficient to constitute a recognition of the compound as a result effective variable.

The Applicants note that the Examiner has cited to Wise and Li as teaching that sodium bicarbonate can be used as an expandable agent and that such can control porosity. However, Applicants maintain that the primary reference, Royer, does not disclose such a use and neither reference, Wise nor Li, recognizes the effect of an expandable agent on curing times as presently claimed. As such, the presently recited amounts of expandable agent, sorbed aqueous medium, and biodegradable hydrating ceramics in an injectable composition are not recognized in the art as result effective variables for the presently claimed curing times.

In addition to the above, Applicants note that Royer is generally directed towards inorganic-polymer complexes for the controlled release of compounds including medicinals. Abstract. Specifically, rather than controlling release through the matrix, Royer uses a "complexing agent" "capable of aggregation which has an affinity for the active agent." Paragraph [0018]. As such, Applicants note that the mechanism described in Royer for controlling its release kinetics is different than that presently claimed that uses an injectable composition that solidifies with a ruptured structure thereby determining the release profile of the active substance.

In light of these disparate mechanisms for controlling the release, Applicants submit that Royer actually teaches away from the present invention. As Applicants have raised the issue of teaching away, the Applicants would like to review the current case law regarding teaching away for the Examiner's convenience. The Court of Appeals for the Federal Circuit has clearly stated

that “an applicant may rebut a *prima facie* case of obviousness by showing that the prior art teaches away from the claimed invention in any material respect.” *In re Petersen*, 315 F.3d 1325, 1331 (Fed. Cir. 2003). The Court has also stated that “[w]e have noted elsewhere, as a ‘useful general rule,’ that references that teach away cannot serve to create a *prima facie* case of obviousness.” (emphasis added) *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1354 (Fed. Cir. 2001). In identifying the appropriate standard for teaching away, the Court has further stated:

“A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be **discouraged from following the path set out in the reference**, or would be led in a **direction divergent** from the **path** that was **taken by the applicant**. The degree of teaching away will of course depend on the particular facts; in general, a reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant.” (emphasis added) *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994).

Clearly in the present case, a person of ordinary skill in the art would be led on a path divergent from the path taken by Applicant as Royer teaches the use of a complexing agent to control release kinetics (see [0016-0018]) while the present invention utilizes an injectable pharmaceutical composition including a biodegradable hydrating ceramic, an expandable agent, and sorbed aqueous medium, providing a solid form with a ruptured structure.

For all of the foregoing reasons, Applicants submit that no *prima facie* case of obviousness has been established with respect to the pending claims, as the present combination of references does not teach each and every element of the currently amended claims, the art does not recognize the presently recited amounts as a result effective variable for achieving the presently recited curing time, and as Royer (the primary reference) teaches away from the present invention. Therefore, Applicants respectfully request withdrawal of the rejection.

Claims 74 and 75 were rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Royer, Wise, and Li in view of Stupak. First, Applicants renew their arguments set forth above with respect to the failure to establish a *prima facie* case of obviousness over claim 73.

Further, Applicants submit that nothing in the cited references teaches or suggests anything that would motivate one of ordinary skill in the art to deliver the active agents taught by Stupak as being deliverable orally in a composition intended for use in repairing periodontal defects, orthopedic defects, root canals, extraction sockets, and screw channels. Thus, Applicants submit that no *prima facie* case of obviousness has been established with respect to claims 74 and 75 and they respectfully request withdrawal of the rejection.

Claims 100-106 were rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Royer, Wise, and Li in view of Ashton. First, Applicants renew their arguments set forth above with respect to the failure to establish a *prima facie* case of obviousness over claim 73. Further, Applicants note that although Ashton teaches pore sealing agents, such agents are taught for use in sealing the pores of medical devices such as stents and not for use in pharmaceutical compositions. Accordingly, Applicants submit that one of ordinary skill in the art would not logically combine the teachings of Ashton with Royer, Wise, and Li in order to arrive at the claimed invention. Further, Applicants note that Example 15 of Royer, the only example that teaches a compound that could be construed as an expandable agent, expressly teaches that the role of the composition is to form “porous orthopedic filler” and that the porosity of the composition “allows the penetration of cells.” Thus, Applicants submit that even assuming, *arguendo*, that Ashton and Royer are sufficiently close in their field of art that one of ordinary skill might look to Ashton, such a person would not be inclined to combine the teachings of Ashton with Example 15 of Royer because such a combination would inherently destroy the functionality of the composition of Example 15. Inherently the role of a pore sealing agent is to seal the pores in a material, while the purpose of Royer’s Example 15 is to produce a “Porous Orthopedic Filler” that “allows the penetration of cells.” Thus, a combination of the two would result in a composition that had clogged or sealed pores that would not allow for the desired passage of cells, thereby destroying the functionality of Royer’s composition. Accordingly, for all of the foregoing reasons, Applicants submit that no *prima facie* case of obviousness has been established. Withdrawal of the rejection is requested.

CONCLUSION

In light of the above, Applicant respectfully submits that pending claims 73-89, 92-97, and 99-116 are now in condition for allowance. Therefore, Applicant requests that the rejections and objections be withdrawn, and that the claims be allowed and passed to issue. If any impediment to the allowance of these claims remains after entry of this Amendment, the Examiner is strongly to call the undersigned attorney at (801) 566-6633 so that such matters may be resolved as expeditiously as possible.

The Commissioner is hereby authorized to charge any additional fee or to credit any overpayment in connection with this Amendment to Deposit Account No. 20-0100.

DATED this 17th day of June, 2011.

Respectfully submitted,

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